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L3 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:844018 CAPLUS

TI Metallosupramolecular Chemistry in Two Dimensions AU Schuette, Markus; Stolle, Christa; Kurth, Dirk G. CS Research Campus Golm, Max Planck Institute of Colloids and Interfaces, Potsdam, D-14424, Germany SO Supramolecular Chemistry (2003), 15(7-8), 549-555 CODEN:

SCHEER; ISSN: 1061-0278 PB Taylor & Francis Ltd.

DT Journal

LA English

AB Ultrathin films of metallosupramol. coordination polyelectrolytes (MEPEs) on planar solid substrates assembled by electrostatic layer-by-layer self-assembly (ELSA) are characterized with UV-vis spectroscopy, optical ellipsometry, and X-ray reflectometry. MEPEs based on different ditopic ligands and transition metal ions are employed and shown to form regular ELSA multilayers. A quant. anal. is in agreement with a surface coverage of approx. two \*\*\*MEPE\*\*\* monolayers per deposition step. In addn., we demonstrate that multilayers of MEPEs with different transition metal ions can be assembled. Even with kinetically labile metal ions, there is no metal ion exchange in these multilayers. Absorption spectra of multilayers on silicon show a band inversion of the MLCT band, which is rationalized in terms of optical effects.

L3 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:749612 CAPLUS DN 139:259403

TI Regulation of Fibroblastic Growth Factor 23 Expression but Not Degradation by  $\ensuremath{\mathsf{PHEX}}$ 

AU Liu, Shiguang; Guo, Rong; Simpson, Leigh G.; Xiao, Zhou-Sheng; Burnham, Charles E.; Quarles, L. Darryl CS Center for Bone and Mineral Disorders, Department of Medicine, Duke University Medical Center, Durham, NC, 27710,

SO Journal of Biological Chemistry (2003), 278(39), 37419-37426 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology DT Journal

LA English

AB Inactivating mutations of Phex cause X-linked hypophosphatemia (XLH) by increasing levels of a circulating phosphaturic factor. FGF23 is a candidate for this phosphaturic factor. Elevated serum FGF23 levels correlate with the degree of hypophosphatemia in XLH, suggesting that loss of Phex function in this disorder results in either diminished degrdn. and/or increased biosynthesis of FGF23. To establish the mechanisms whereby Phex regulates FGF23, the authors assessed Phexdependent hydrolysis of recombinant FGF23 in vitro and measured fgf23 message levels in the Hyp mouse homolog of XLH. In COS-7 cells, overexpression of FGF23 resulted in its degrdn. into N- and C-terminal fragments by an endogenous decanoyl-Arg-Val-Lys-Arg-chloromethyl ketone-sensitive furintype convertase. Phex-dependent hydrolysis of full-length FGF23 or its N- and C-terminal fragments could not be demonstrated in the presence or absence of decanovi-Arg-Val-Lys-Argchloromethyl ketone in COS-7 cells expressing Phex and FGF23. In a reticulolyzate system, apparent cleavage of FGF23 occurred with wild-type Phex, the inactive Phex-3'M mutant, and vector controls, indicating nonspecific metab. of FGF23 by contaminating enzymes. These findings suggest that FGF23 is not a direct Phex substrate. In contrast, by real-time reverse transcriptase PCR, the levels of fgf23 transcripts were highest in bone, the predominant site of Phex expression. In addn., Hyp mice displayed a bone-restricted increase in fgf23 transcripts in assocn, with inactivating Phex mutations. Increased expression of fgf23 was also obsd. in Hyp-derived osteoblasts in culture. These findings suggest that Phex, possibly through the actions of unidentified Phex substrates or other downstream effectors. regulates fgf23 expression as part of a potential hormonal axis between bone and kidney that controls systemic phosphate homeostasis and mineralization.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:736619 CAPLUS

TI Motorcycle exhaust particulates enhance vasoconstriction in organ culture of rat aortas and involve reactive oxygen species AU Tzeng, Hui-Ping; Yang, Rong-Sen; Ueng, Tzuu-Huei; Lin-Shiau, Shoei-Yn; Liu, Shing-Hwa

CS Institute of Toxicology, College of Medicine, National Taiwan University, Taipei, Taiwan

SO Toxicological Sciences (2003), 75(1), 66-73 CODEN: TOSCF2; ISSN: 1096-6080

**PB Oxford University Press** 

DT Journal

LA English

AB The effects of motorcycle exhaust particulate on vasoconstriction were detd. using rat thoracic aortas under organ culture conditions treated with org. exts. of motorcycle exhaust particulate from a two-stroke engine. The motorcycle exhaust particulate ext. ( \*\*\*MEPE\*\*\* ) induced a concn.-dependent enhancement of vasoconstriction elicited by phenylephrine in the organ cultures of both intact and endothelium-denuded aortas for 18 h. Nifedipine (an L-type Ca2+ channel blocker), manganese acetate (an inorg. Ca2+ channel blocker), and staurosporine (a nonselective protein kinase C inhibitor), but not the selective protein kinase C inhibitor chelerythrine, inhibited the enhancement of vasoconstriction by \*\*\*MEPE\*\*\* . Staurosporine has also been reported as a myosin light chain kinase (MLCK) inhibitor, so we tested whether the MLCK pathway was involved in the effect of \*\*\*MEPE\*\*\* . The results showed that ML-9 (a selective MLCK inhibitor) could inhibit the enhancement of vasoconstriction by \*\*\*MEPE\*\*\* . The phosphorylation of a 20kDa myosin light chain in a primary culture of rat vascular

smooth muscle cells was also enhanced by \*\*\*MEPE\*\*\*. Moreover, we also examd. the role of reactive oxygen species (ROS) in the stimulatory effect of \*\*\*MEPE\*\*\* on vasoconstriction. The antioxidant N-acetylcysteine significantly inhibited the enhancement of vasoconstriction by \*\*\*MEPE\*\*\*. A time-dependent increase in ROS prodn. by \*\*\*MEPE\*\*\* was also detected in primary cultures of vascular smooth muscle cells. These results indicate that \*\*\*MEPE\*\*\* induces a marked enhancement of vasoconstriction in aortas under organ culture conditions and imply that a ROS-Ca2+-MLCK pathway may be involved in this \*\*\*MEPE\*\*\* -induced response.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:561476 CAPLUS

DN 139:302120

TI FGF23, PHEX, and \*\*\*MEPE\*\*\* regulation of phosphate homeostasis and skeletal mineralization

AU Quarles, L. Darryl

CS Department of Medicine, Center for Bone and Mineral Disorders, Duke University Medical Center, Durham, NC, 27710, USA

SO American Journal of Physiology (2003), 285(1, Pt. 1), E1-E9 CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal; General Review

LA English

AB A review. There is evidence for a hormone/enzyme/extracellular matrix protein cascade involving fibroblastic growth factor 23 (FGF23), a phosphate-regulating gene with homologies to endopeptidases on the X chromosome (PHEX), and a matrix extracellular phosphoglycoprotein ( \*\*\*MEPE\*\*\* ) that regulates systemic phosphate homeostasis and mineralization. Genetic studies of autosomal dominant hypophosphatemic rickets (ADHR) and X-linked hypophosphatemia (XLH) identified the phosphaturic hormone FGF23 and the membrane metalloprotease PHEX, and investigations of tumor-induced osteomalacia (TIO) discovered the extracellular matrix protein \*\*\*MEPE\*\*\* . Similarities between ADHR, XLH, and TIO suggest a model to explain the common pathogenesis of renal phosphate wasting and defective mineralization in these disorders. In this model, increments in FGF23 and \*\*\*MEPE\*\*\*, resp., cause renal phosphate wasting and intrinsic mineralization abnormalities. FGF23 elevations in ADHR are due to mutations of FGF23 that block its degrdn., in XLH from indirect actions of inactivating mutations of PHEX to modify the expression and/or degrdn. of FGF23 and \*\*\*MEPE\*\*\* , and in TIO because of increased prodn. of FGF23 and \*\*\*MEPE\*\*\* . Although this model is attractive, several aspects need to be validated. First, the enzymes responsible for metabolizing FGF23 and \*\*\*MEPE\*\*\* need to be established. Second, the physiol. relevant PHEX substrates and the mechanisms whereby PHEX controls FGF23 and \*\*\*MEPE\*\*\* metab. need to be elucidated. Finally, addnl. studies are required to establish the mol. mechanisms of FGF23 and \*\*\*MEPE\*\*\* actions on kidney and bone, as well as to confirm the role of these and other potential "phosphatonins," such as frizzled related protein-4, in the pathogenesis of the renal and skeletal phenotypes in XLH and TIO. Unraveling the components of this hormone/enzyme/extracellular matrix pathway will not only lead to a better understanding of phosphate homeostasis and mineralization but may also improve the diagnosis and treatment of hypo- and hyperphosphatemic disorders. RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR

THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:483474 CAPLUS

DN 140:14264

TI Human recombinant endopeptidase PHEX has a strict S1' specificity for acidic residues and cleaves peptides derived from fibroblast growth factor-23 and matrix extracellular phosphoglycoprotein

AU Campos, Marcelo; Couture, Constance; Hirata, Izaura Y.; Juliano, Maria A.; Loisel, Thomas P.; Crine, Philippe; Juliano, Luiz; Boileau, Guy; Carmona, Adriana K.

CS Escola Paulista de Medicina, Department of Biophysics, Universidade Federal de Sao Paulo, Sao Paulo, 04044-020, Brazil SO Biochemical Journal (2003), 373(1), 271-279 CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.

DT Journal

LA English

AB The PHEX gene (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) encodes a protein (PHEX) with structural homologies to members of the M13 family of zinc metallo-endopeptidases. Mutations in the PHEX gene are responsible for X-linked hypophosphatemia in humans. However, the mechanism by which loss of PHEX function results in the disease phenotype, and the endogenous PHEX substrate(s) remain unknown. In order to study PHEX substrate specificity, combinatorial fluorescent-quenched peptide libraries contg. oaminobenzoic acid (Abz) and 2,4-dinitrophenyl (Dnp) as the donor-acceptor pair were synthesized and tested as PHEX substrates. PHEX showed a strict requirement for acidic amino acid residues (aspartate or glutamate) in S1' subsite, with a strong preference for aspartate. Subsites S2', S1 and S2 exhibited less defined specificity requirements, but the presence of leucine, proline or glycine in P2', or valine, isoleucine or histidine in P1 precluded hydrolysis of the substrate by the enzyme. The peptide Abz-GFSDYK(Dnp)-OH, which contains the most favorable residues in the P2 to P2' positions, was hydrolyzed by PHEX at the N-terminus of aspartate with a k cat/ K m of 167 mM-1.cntdot.s-1. In addn., using quenched fluorescence peptides derived from fibroblast growth factor-23 and matrix extracellular phosphoglycoprotein sequences flanked by Abz and N -(2,4dinitrophenyl)ethylenediamine, we showed that these physiol. relevant proteins are potential PHEX substrates. Finally, our results clearly indicate that PHEX does not have neprilysin-like substrate specificity.

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:397883 CAPLUS

DN 139:157589

TI Electron crystallography on polymorphic organics AU Kolb, U.; Matveeva, G. N.

CS Institut fur Physikalische Chemie, Welderweg 11, Johannes Gutenberg-Universitat, Mainz, D-55099, Germany

SO Zeitschrift fuer Kristallographie (2003), 218(4), 259-268

CODEN: ZEKRDZ; ISSN: 0044-2968

PB Oldenbourg Wissenschaftsverlag GmbH

**DT** Journal

LA English

AB Org. materials, such as nonlinear optical active compds. (1-(2furyl)-3-(4-aminophenyl)-2-propene-1-one (FAPPO) and 1-(2furyl)-3-(4-benzamidophenyl)-2-propene-1-one (FBAPPO)), polymeric materials like the metal coordinated polyelectrolyte (Fe(II) [ditopic bis-terpyridin] ( \*\*\*MEPE\*\*\* )) or polymorphic materials (e.g. Cu-phthalocyanine), which do not crystallize big enough for single crystal x-ray structure anal. were investigated by electron diffraction (ED) at 100 and 300 kV acceleration

voltage. Sample prepn. (direct crystn., ultra sonication, ultra microtomy), diffraction strategies (selected area diffraction, nano diffraction, use of double-tilt rotation holder), data collection and data processing as well as structure soln, strategies were chosen dependent on the different requirements of the compds, under investigation. Structure anal. was carried out by simulation using ab initio quantum-mech. methods like d. functional theory (DFT), semi-empirical approach (MNDO/AM1/PM3) and force field packing energy calcns. (DREIDING). The structure models resulting from simulation were refined kinematically as rigid bodies. Subsequently, refinements by multi-slice least squares (MSLS) procedures taking dynamical scattering into account were performed. The described combination of different methods which was used successfully on crystallizable materials is also adaptable to insol. org. materials (e.g. pigments) and polymorphic systems.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:381234 CAPLUS

DN 138:338994

TI Metalio-supramolecular polyelectrolyte multilayers with cobalt(II): preparation and properties AU Kurth, Dirk G.

CS Mac-Planck-Inst. of Colloids and Interfaces, Potsdam, D-14476, Germany

SO Polymeric Materials Science and Engineering (2001), 84, 245-246 CODEN: PMSEDG; ISSN: 0743-0515

**PB American Chemical Society** 

DT Journal

LA English

AB Metal ion mediated self-assembly of the ditopic ligand 1,4bis(2,2':6',2"-terpyridine-4'-yl)benzene and Co(II) results in a metallo-supramol. coordination polyelectrolyte (Co- \*\*\*MEPE\*\*\* ), which is analyzed by spectroscopic methods and cyclic voltammetry. The Co- \*\*\*MEPE\*\*\* shows a pronounced pair of current waves with a half-wave potential of 87 mV. Thin films of Co- \*\*\*MEPE\*\*\* are fabricated by layer-by-layer self-assembly together with poly(styrenesulfonate) (PSS) on planar substrates and are analyzed by UV/vis spectroscopy and electrochem. The Co-ions in the multilayer can be removed and displaced by Feions. The electrochem, activity of the Co-ions is fully maintained in the films. The permeability of the multilayers is investigated by electrochem. using K3[Fe(CN)6] as electroactive probe. Compared to poly(allylamine hydrochloride) (PAH)/PSS films, the electroactive probe does not permeate through PSS/Co-\*\*\*MEPE\*\*\* multilayers.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:332491 CAPLUS

DN 139:129584

TI Six Genes Expressed in Bones and Teeth Encode the Current Members of the SIBLING Family of Proteins

AU Fisher, Larry W.; Fedarko, Neal S.

CS Matrix Biochemistry Unit, HHS, NIDCR, Craniofacial & Skeletal Diseases Branch, NIH, Bethesda, MD, USA

SO Connective Tissue Research (2003), 44(Suppl. 1), 33-40 CODEN: CVTRBC; ISSN: 0300-8207

PB Taylor & Francis, Inc.

DT Journal

LA English

AB Bone sialoprotein (BSP), dentin matrix protein 1 (DMP1), dentin sialophosphoprotein (DSPP), enamelin (ENAM), matrix extracellular phosphoglycoprotein ( \*\*\*MEPE\*\*\* ), and

osteopontin (OPN) are glycophosphoproteins expressed in bones and/or teeth. Direct comparison of their amino acid sequences do not suggest that they belong to a single genetic family, but a detailed anal, of their chromosomal location and gene structure does. Anal. of human brain mRNA by RT-PCR has led to the discovery of two addnl. exons thereby making it more convincing that \*\*\*MEPE\*\*\* is a member of the SIBLING (Small Integrin-Binding LIgand, N-linked Glycoprotein) family. We propose that the members of this SIBLING family are extended, flexible proteins in soln. that can facilitate the formation of a no. of different complexes. For example, OPN can bridge complement Factor H to either an RGD-dependent integrin or to CD44 forming a membrane-bound complex that actively suppresses the alternate complement pathway. Two possible mechanisms for inhibiting the lytic pathway of alternate complement are presented.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2003:290990 CAPLUS

DN 139:18114

TI Mineralized tissue and vertebrate evolution: The secretory calcium-binding phosphoprotein gene cluster

AU Kawasaki, Kazuhiko; Weiss, Kenneth M.

CS Department of Anthropology, Pennsylvania State University, University Park, PA, 16802, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(7), 4060-4065 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Gene duplication creates evolutionary novelties by using older tools in new ways. The authors have identified evidence that the genes for enamel matrix proteins (EMPs), milk caseins, and salivary proteins comprise a family descended from a common ancestor by tandem gene duplication. These genes remain linked, except for one EMP gene, amelogenin. These genes show common structural features and are expressed in ontogenetically similar tissues. Many of these genes encode secretory Ca-binding phosphoproteins, which regulate the Ca-phosphate concn. of the extracellular environment. By exploiting this fundamental property, these genes have subsequently diversified to serve specialized adaptive functions. Casein makes milk supersatd, with Ca-phosphate, which was crit. to the successive mammalian divergence. The innovation of enamel led to mineralized feeding app., which enabled active predation of early vertebrates. The EMP genes comprise a subfamily not identified previously. A set of genes for dentin and bone extracellular matrix proteins constitutes an addnl. cluster distal to the EMP gene cluster, with similar structural features to EMP genes. The duplication and diversification of the primordial genes for enamel/dentin/bone extracellular matrix may have been important in core vertebrate feeding adaptations, the mineralized skeleton, the evolution of saliva, and, eventually, lactation. The order of duplication events may help delineate early events in mineralized skeletal formation, which is a major characteristic of vertebrates. RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR

THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
L3 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:25883 CAPLUS

DN 139:4220

TI Targeted Disruption of the Osteoblast/Osteocyte Factor 45 Gene (OF45) Results in Increased Bone Formation and Bone Mass AU Gowen, Lori C.; Petersen, Donna N.; Mansolf, Amy L.; Qi, Hong; Stock, Jeffrey L.; Tkalcevic, George T.; Simmons, Hollis A.; Crawford, David T.; Chidsey-Frink, Kristen L.; Ke, Hua Zhu; McNeish, John D.; Brown, Thomas A.

CS Department of Cardiovascular and Metabolic Diseases, Pfizer Global Research and Development, Groton, CT, 06340, USA SO Journal of Biological Chemistry (2003), 278(3), 1998-2007 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology DT Journal

LA English

AB We have previously described osteoblast/osteocyte factor 45 (OF45), a novel bone-specific extracellular matrix protein, and demonstrated that its expression is tightly linked to mineralization and bone formation. In this report, we have cloned and characterized the mouse OF45 cDNA and genomic region. Mouse OF45 (also called \*\*\*MEPE\*\*\* ) was similar to its rat ortholog in that its expression was increased during mineralization in osteoblast cultures and the protein was highly expressed within the osteocytes that are imbedded within bone. To further det. the role of OF45 in bone metab., we generated a targeted mouse line deficient in this protein. Ablation of OF45 resulted in increased bone mass. In fact, disruption of only a single allele of OF45 caused significantly increased bone mass. In addn., knockout mice were resistant to aging-assocd. trabecular bone loss. Cancellous bone histomorphometry revealed that the increased bone mass was the result of increased osteoblast no. and osteoblast activity with unaltered osteoclast no. and osteoclast surface in knockout animals. Consistent with the bone histomorphometric results, we also detd. that OF45 knockout osteoblasts produced significantly more mineralized nodules in ex vivo cell cultures than did wild type osteoblasts. Osteoclastogenesis and bone resorption in ex vivo cultures was unaffected by OF45 mutation. We conclude that OF45 plays an

inhibitory role in bone formation in mouse.

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR

THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:963313 CAPLUS

DN 138:151566

TI Partial rescue of the Hyp phenotype by osteoblast-targeted PHEX (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) expression AU Bai, Xiuying; Maio, Dengshun; Panda, Dibiyendu; Grady, Scott; McKee, Marc D.; Goltzman, David; Karaplis, Andrew C. CS Division of Endocrinology, Department of Medicine, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montreal, QC, H3T 1E2, Can.

SO Molecular Endocrinology (2002), 16(12), 2913-2925 CODEN: MOENEN; ISSN: 0888-8809

PB Endocrine Society

DT Journal

LA English

AB Inactivating mutations and/or deletions of PHEX/Phex (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) are responsible for X-linked hypophosphatemic rickets in humans and in the murine homolog Hyp. The predominant osteoblastic expression of Phex has implicated a primary metabolic osteoblast defect in the pathophysiol. of this disorder. By targeting PHEX expression to osteoblasts in the Hyp genetic background, the authors aimed to correct the corresponding biochem. and morphol. abnormalities and obtain information on their pathogenetic mechanism. When transgene Phex expression, driven by a mouse pro-alpha.1(1) collagen gene promoter, was crossed into the Hyp background, it improved the defective mineralization of bone and teeth but

failed to correct the hypophosphatemia and altered vitamin D metab. assocd. with the disorder. Ex vivo bone marrow cultures confirmed the amelioration in the Hyp-assocd. matrix mineralization defect after Phex expression. These findings suggest that while the Hyp bone and teeth abnormalities partially correct after PHEX gene transfer, addnl. factors and/or sites of PHEX expression are likely crit. for the elaboration of the appropriate mol. signals that alter renal phosphate handling and vitamin D metab. in this disorder.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:665448 CAPLUS

DN 138:23101

TI Inhibition of \*\*\*MEPE\*\*\* cleavage by Phex

AU Guo, Rong; Rowe, Peter S. N.; Liu, Shiguang; Simpson, Leigh G.; Xiao, Zhou-Sheng; Darryl Quarles, L.

CS The Center for Bone and Mineral Disorders, Department of Medicine, Duke University Medical Center, Durham, NC, 27710, LISA

SO Biochemical and Biophysical Research Communications (2002), 297(1), 38-45 CODEN: BBRCA9; ISSN: 0006-291X PB Elsevier Science

DT Journal

LA English

AB X-linked hypophosphatemia (XLH) and the Hyp-mouse disease homolog are caused by inactivating mutations of Phex which results in the local accumulation of an unknown autocrine/paracrine factor in bone that inhibits mineralization of extracellular matrix. In these studies, we evaluated whether the matrix phosphoglycoprotein \*\*\*MEPE\*\*\*, which is increased in calvaria from Hyp mice, is a substrate for Phex. Using recombinant full-length Phex (rPhexWT) produced in Sf9 cells, we failed to observe Phex-dependent hydrolysis of recombinant human \*\*\*MEPE\*\*\* (rMEPE). Rather, we found that rPhex-WT inhibited cleavage of rMEPE by endogenous cathepsin-like enzyme activity present in Sf9 membrane. Sf9 membranes as well as purified cathepsin B cleaved \*\*\*MEPE\*\*\* into two major fragments of .apprx.50 and .apprx.42 kDa. RPhexWT protein in Sf9 membrane fractions, co-incubation of rPhexWT and cathepsin B, and pre-treatment of Sf9 membranes with leupeptin prevented the hydrolysis of \*\*\*MEPE\*\*\* in vitro. The C-terminal domain of Phex was required for inhibition of \*\*\*MEPE\*\*\* cleavage, since the C-terminal deletion mutant rPhex (1-433) [rPhex3'M] failed to inhibit Sf9-dependent metab. of \*\*\*MEPE\*\*\* . Phex-dependent inhibition of \*\*\*MEPE\*\*\* degrdn., however, did not require Phex enzymic activity, since EDTA, an inhibitor of rPhex, failed to block rPhexWT inhibition of \*\*\*MEPE\*\*\* cleavage by Sf9 membranes. Since we were unable to identify interactions of Phex with \*\*\*MEPE\*\*\* or actions of Phex to metabolize cathepsin B, Phex may be acting to interfere with the actions of other enzymes that degrade extracellular matrix proteins. Although the mol. mechanism and biol. relevance of non-enzymic actions of Phex need to be established, these findings indicate that \*\*\*MEPE\*\*\* may be involved in the pathogenesis of defective mineralization due to Phex deficiency in XLH and the Hyp-mouse.

L3 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:622275 CAPLUS DN 138:84177

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR

THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI \*\*\*MEPE\*\*\* /OF45, a new dentin/bone matrix protein and candidate gene for dentin diseases mapping to chromosome 4q21

AU MacDougall, Mary; Simmons, Darrin; Gu, Ting Ting; Dong, Juan

CS Department of Pediatric Dentistry, Dental School, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78229-3900, USA

SO Connective Tissue Research (2002), 43(2-3), 320-330 CODEN: CVTRBC; ISSN: 0300-8207

PB Taylor & Francis Ltd.

DT Journal

LA English

AB Substantial progress has been made regarding the mol. etiol. of the dentin diseases dentinogenesis imperfecta types II and III, and dentin dysplasia type II. Genetic linkage studies have identified the crit. loci for these diseases on human chromosome 4q21. Located within an overlapping segment of these disease loci is a dentin/bone gene cluster that includes osteopontin, bone sialoprotein, dentin matrix protein 1, dentin sialophosphoprotein. and a new gene \*\*\*MEPE\*\*\* also known as OF45, renamed osteoregulin. In this paper, we report the location of \*\*\*MEPE\*\*\* /OF45 in relationship to the other members of the dentin/bone gene cluster as well as the genomic organization of the human gene. For the first time, \*\*\*MEPE\*\*\* /OF45 expression was shown in dental tissue, in particular odontoblasts. by reverse-transcription polymerase chain reaction (RT-PCR) amplification and characterization of a partial mouse cDNA. Our data provide the first evidence that \*\*\*MEPE\*\*\* /OF45 is expressed during odontogenesis and should be considered as a candidate gene for dentin structural diseases mapping to human chromosome 4a21. RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR

THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:461775 CAPLUS DN 137:276731

TI Tumors associated with oncogenic osteomalacia express genes important in bone and mineral metabolism

AU Jan De Beur, Suzanne M.; Finnegan, Richard B.; Vassiliadis, John; Cook, Brian; Barberio, Dana; Estes, Scott; Manavalan, Partha; Petroziello, Joseph; Madden, Stephen L.; Cho, Justin Y.; Kumar, Rajiv; Levine, Michael A.; Schiavi, Susan C. CS Department of Medicine, Johns Hopkins University School of

CS Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

SO Journal of Bone and Mineral Research (2002), 17(6), 1102-1110 CODEN: JBMREJ; ISSN: 0884-0431

PB American Society for Bone and Mineral Research DT Journal

LA English

AB Oncogenic osteomalacia (OOM) is assocd. with primitive mesenchymal tumors that secrete phosphaturic factors resulting in low serum concns. of phosphate and calcitriol, phosphaturia, and defective bone mineralization. To identify overexpressed genes in these tumors, the authors compared gene expression profiles of tumors resected from patients with OOM and histol. similar control tumors using serial anal, of gene expression (SAGE). Three hundred and sixty-four genes were expressed at least twofold greater in OOM tumors compared with control tumors. A subset of 67 highly expressed genes underwent validation with an extended set of OOM and control tumors using array anal. or reverse-transcription polymerase chain reaction (RT-PCR). Ten of these validated genes were consistently overexpressed in all OOM tumors relative to control tumors. Strikingly, genes with roles in bone matrix formation, mineral ion transport, and bone mineralization were highly expressed in the OOM tumors.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:409484 CAPLUS

DN 138:127311

 $\Pi$  Metallosupramolecular coordination polyelectrolytes. Potential building blocks for molecular-based devices

AU Kurth, Dirk G.

CS Max Planck Institute of Colloids and Interfaces, Potsdam, D-14424, Germany

SO Annals of the New York Academy of Sciences (2002), 960(Molecular Electronics II), 29-38 CODEN: ANYAA9; ISSN: 0077-8923

PB New York Academy of Sciences

DT Journal; General Review

LA English

AB A review. Metal-ion-induced self-assembly of ditopic ligands, based on bisterpyridines, and transition metal ions gave metallosupramol. coordination polyelectrolytes ( \*\*\*MEPE\*\*\* ). The pos. charge of \*\*\*MEPE\*\*\* can be used in several ways to process highly ordered architectures. Alternating adsorption of \*\*\*MEPE\*\*\* and oppositely charged polyelectrolytes on solid substrates results in multilayers. The sequential nature of this process allows combining MEPEs with other functional components. This process permits nanometer thickness control, is readily adapted for automated processing, and is applicable to 2-dimensional substrates as well as to colloidal templates. The surface chem. properties of \*\*\*MEPE\*\*\* are readily controlled by complexing \*\*\*MEPE\*\*\* with neg. charged amphiphiles. The resulting polyelectrolyte amphiphile complexes (PAC) are sol, in org. solvents and form liq. cryst. phases. The PAC also spreads at the air-H2O interface as Langmuir monolayer, which can be transferred onto solid substrates. The resulting Langmuir-Blodgett multilayers are highly ordered and anisotropic. Materials with transition metal ions possess many interesting properties, including spin transitions, magnetism, as well as photochem. assets that are relevant for the construction of functional devices and materials. The presented approach combines principles of supramol, and colloidal chem, as well as surface science, is highly modular, and provides extensive control of structure and function from mol. to macroscopic levels.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:348403 CAPLUS

DN 137:43047

TI An introduction to the SIBLING family of proteins AU Fisher, Larry W.; Fedarko, Neal S.

CS Matrix Biochemistry Unit, Craniofacial and Skeletal Diseases Branch, NIDCR, NIH, Bethesda, MD, 20892-4320, USA SO TheScientificWorld [online computer file] (2002), 2, 22-24 CODEN: THESAS; ISSN: 1532-2246 URL:

http://216.25.253.202/TSWJaudit/pdf/2002.27.240.pdf PB TheScientificWorld, Inc.

DT Journal; General Review; (online computer file) LA English

AB A review. Characteristics of the protein family called SIBLING (small integrin-binding ligands and N-linked glycoproteins) are described. Currently there are 5 members of the family: osteopontin (OPN), bone sialoprotein (BSP), dentin matrix protein 1 (DMP1), dentin sialophosphoprotein (DSPP), and matrix extracellular phosphoglycoprotein (\*\*\*MEPE\*\*\*). All these proteins are expressed in bones and/or teeth. All 5 genes are clustered within a 800,000 basepair region of human chromosome 4 (mouse chromosome 5). The functional domains of the exons are highly conserved. All introns interrupt exons between codons (type 0) suggesting that any splice variant keeps

reading frame intact. Post-translational modifications and binding properties of BSP and OPN were studied.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L3 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2002:142293 CAPLUS

DN 136:392326

TI Metallo-supramolecular polyelectrolyte multilayers with cobalt(II): preparation and properties
AU Kurth, Dirk G.; Schutte, Markus; Wen, Jin
CS Max-Planck-Institute of Colloids and Interfaces, Potsdam, 14424, Germany

SO Colloids and Surfaces, A: Physicochemical and Engineering Aspects (2002), 198-200, 633-643 CODEN: CPEAEH; ISSN: 0927-7757

PB Elsevier Science B.V.

DT Journal

LA English

AB Metal ion mediated self-assembly of the ditopic ligand 1,4bis(2,2':6',2"-terpyridine-4'-yl)benzene and Co(II) results in a metallosupramol. coordination polyelectrolyte (Co- \*\*\*MEPE\*\*\* ), which is analyzed by spectroscopic methods, elemental anal. and cyclic voltammetry. The Co- \*\*\*MEPE\*\*\* shows a reversible one-electron redox transition in the potential range from -0.15 to 0.35 V with a half-wave potential of 87 mV. Thin films of Co-\*\*\*MEPE\*\*\* are fabricated by layer-by-layer self-assembly together with poly(styrenesulfonate) (PSS) on planar substrates and are analyzed by UV/vis spectroscopy, microgravimetry, and electrochem. The Co-ions in the multilayer can be removed and displaced by Fe-ions. The electrochem. activity of the Co-ions is fully maintained in the films. Charge transport through the multilayer is consistent with electron self-exchange reactions. The permeability of the multilayers is investigated by electrochem. using K3[Fe(CN)6] as electroactive probe. Compared to poly(allylamine hydrochloride) (PAH)/PSS films, the electroactive probe does not permeate through PSS/Co- \*\*\*MEPE\*\*\* multilayers. Fluorescence measurements with pyrene as polarity probe indicate that the Co- \*\*\*MEPE\*\*\* films are more hydrophobic than PAH/PSS multilayers.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:689186 CAPLUS

DN 136:30126

 $\Pi$  Models for description of the influence of light intensity on the parameters of the transient photo-EMF of organic photoconductors

AU Damm, Cornelia; Werner Mueller, F.; Israel, Gunter CS Institut fur Organische Chemie, Martin-Luther-Universitaet Halle-Wittenberg, Merseburg, 06217, Germany SO Physical Chemistry Chemical Physics (2001), 3(18), 4096-4101 CODEN: PPCPFQ; ISSN: 1463-9076 PB Royal Society of Chemistry

DT Journal

LA English

AB The aim of this work is a quant. description of the connections between the excitation laser flash intensity and the parameters of the transient photo-EMF. The models suggested in this paper were checked by exptl. data obtained from layers of the org. photoconductors N,N'- dimethylperylenetetracarboxylic bisimide (\*\*\*MePe\*\*\*, n-type photoconductor) and Cu(II) phthalocyanine (CuPc, p-type photoconductor) dispersed in poly(vinyl butyrale) (PVB) as binder. The models used are valid both for a neglectable and for a real dark charge carrier concn. Nevertheless, recombination is the most important pathway of charge carrier

disappearance in both photoconductors. The models may also describe the influence of laser flash intensity if the sample is illuminated by continuous white Xe light addnl. to the laser flash and also if the laser is focused on a very small sample area. The model valid for a real dark charge carrier concn. yields the best reprodn. of the exptl. data. In the case of neglectable dark charge carrier concns. this model may be simplified. Then it permits an estn. of the mobility ratio of electrons and holes .mu.n/.mu.p: for example at excitation wavelength .lambda. flash = 580 nm the ratio .mu.n/.mu.p amts. to 1.35 for \*\*\*MePe\*\*\* and 0.73 for CuPc.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:444217 CAPLUS

DN 136:162014

TI \*\*\*MEPE\*\*\*, the gene encoding a tumor-secreted protein in oncogenic hypophosphatemic osteomalacia, is expressed in bone AU Argiro, L.; Desbarats, M.; Glorieux, F. H.; Ecarot, B. CS Genetics Unit, Shriners Hospital, Montreal, QC, H3G 1A6, Can. SO Genomics (2001), 74(3), 342-351 CODEN: GNMCEP; ISSN: 0888-7543

**PB Academic Press** 

DT Journal

LA English

AB The \*\*\*MEPE\*\*\* (matrix extracellular phosphoglycoprotein) gene is a strong candidate for the tumor-derived phosphaturic factor in oncogenic hypophosphatemic osteomalacia (OHO), Xlinked hypophosphatemia (XLH) is phenotypically similar to OHO and results from mutations in PHEX, a putative metallopeptidase believed to process a factor(s) regulating bone mineralization and renal phosphate reabsorption. Here we report the isolation of the murine homolog of \*\*\*MEPE\*\*\*, from a bone cDNA library, that encodes a protein of 433 amino acids, 92 amino acids shorter than human \*\*\*MEPE\*\*\* . \*\*\*Mepe\*\*\* , like Phex, is expressed by fully differentiated osteoblasts and down-regulated by 1.25-(OH)2D3. In contrast to Phex, \*\*\*Mepe\*\*\* expression is markedly increased during osteoblast-mediated matrix mineralization. Greater than normal \*\*\*Mepe\*\*\* mRNA levels were obsd. in bone and osteoblasts derived from Hyp mice, the murine homolog of human XLH. Our data provide the first evidence that \*\*\*MEPE\*\*\* / \*\*\*Mepe\*\*\* is expressedby osteoblasts in assocn. with mineralization. (c) 2001 Academic Press.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:316598 CAPLUS

DN 135:66695

TI Structural analysis of a metallosupramolecular polyelectrolyte - amphiphile complex at the air/water interface

AU Lehmann, Pit; Kurth, Dirk G.; Brezesinski, Gerald; Symietz, Christian

CS Max-Planck-Institute of Colloids and Interfaces, Potsdam, 14424, Germany

SO Chemistry--A European Journal (2001), 7(8), 1646-1651 CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

AB A detailed anal. of a metallosupramol. coordination polyelectrolyte - amphiphile complex (PAC) at the air/water interface is presented based on Langmuir isotherm measurements, Brewster angle microscopy as well as x-ray reflectance and diffraction measurements. The PAC was prepd. in

soln. by metal-ion coordination of Fe(OAc)2 and 1,4-bis(2,2':6',2"-terpyridin-4'- yl)benzene followed by self-assembly with dihexadecyl phosphate (DHP). The spreading of the PAC at the air/water interface results in a Langmuir film with a stratified architecture, such that DHP forms a monolayer on the water surface, while the metallosupramol. coordination polyelectrolyte (\*\*\*MEPE\*\*\*) is immersed in the aq. subphase. Electrostatic interactions of \*\*\*MEPE\*\*\* and DHP force the alkyl chains into an upright, hexagonal lattice even at low surface pressures. This work illustrates how supramol., colloidal, and surface chem. can be combined to create complex architectures with tailored characteristics that may not be accessible through self-organization in the liq. phase.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:311975 CAPLUS

DN 134:318534

TI The role of traps in the interpretation of Photo-E.M.F. parameters of organic dye pigments

AU Muller, F. W.; Damm, C.; Israel, G.

CS Martin-Luther-Universitat Halle-Wittenberg, Institut fur Organische Chemie, Merseburg, 06217, Germany

SO Journal of Information Recording (2000), 25(5-6), 611-632 CODEN: JIREFL, ISSN: 1025-6008

PB Gordon & Breach Science Publishers

DT Journal

LA English

AB The decay of the transient Photo-ElectroMotive-Force U (Photo-E.M.F.) of org. dye pigments can be described as a biexponential process even if the signals change the sign of U(t) within the decay. The dependencies of the four parameters U10. U20, k1 and k2 on wavelength and intensity of the exciting laser flash were investigated using Copper(II)-phthalocyanine (CuPc) and N,N'-Dimethylperylene-tetra-carboxylic-bisimide ( \*\*\*MePe\*\*\* ) as pigments dispersed in polyvinyl butyral (PVB) layers. In agreement with the trap concept of MOTT the type of cond. (n- or p-type photoconduction) of \*\*\*MePe\*\*\* depends on the energy of the exciting light. CuPc does not show such a change of the photoconduction. More detailed information about the role of traps available for photogenerated charge carriers electron and hole (e/h) - can be derived from time resolved Photo-E.M.F. expts. under addnl. continuous illumination of the sample by poly- and monochromatic light. The results show, that charge carriers involved in Photo-E.M.F. measurements will be influenced mainly by shallow traps (.DELTA.E in the meV-range). Occupation of traps by charge carriers generated under continuous illumination results in an increase of the decay rate for the faster process. This points out, that its parameters U10 and k1 may be attributed to that Photo-E.M.F. generated near the surface of the pigment particles.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:311966 CAPLUS

DN 134:318533

TI Effects of polymer matrix on the transient Photo-EMF from organic dye pigment layers

AU Damm, C.; Muller, F. W.; Israel, G.

CS Martin-Luther-Universitat Halle-Wittenberg, Institut fur Organische Chemie, Merseburg, D-06217, Germany

SO Journal of Information Recording (2000), 25(5-6), 553-566

CODEN: JIREFL; ISSN: 1025-6008 PB Gordon & Breach Science Publishers

DT Journal

## LA English

AB The influence of the polymer matrix on the parameters of the transient Photo-Electro Motive Force (PEMF) was investigated using Copper(II)-phthalocyanine (CuPc) and N.N'-Dimethylperylenetetracarboxylic- bisimide ( \*\*\*MePe\*\*\* ) pigments in solid pigment-polymer dispersion layers. Different polymers with dielec. consts. .epsilon.r in the range of 2.5-50 were used. The max. voltage UMAX of the PEMF decreased with increasing dielec. const. .epsilon.r as it was expected from the Coulomb law. Unexpectedly there was only a trend in UMAX as a function of 1/.epsilon.r, indicating addnl. influence of the matrix. Sign (+/-) and decay behavior U = f(t) was not influenced by the matrix effects. Action spectra UMAX = f(.lambda.EXC) of \*\*\*MePe\*\*\* /polymer dispersion layers (poly(vinyl butyral), polystyrene, poly(vinyl chloride), cellulose dinitrate) did show a change in sign of PEMF at .lambda.EXC = 600-605 nm independently on the kind of polymer. Using pure matrix-free \*\*\*MePe\*\*\* polycryst. layers (tablets) this change in sign was shifted to .lambda.EXC .gtoreq. 615 nm. Addnl., at .lambda.EXC .gtoreq. 615 nm UMAX was very small and the decay U = f(t)was accelerated. That was attributed to a fast charge transport between the microcrystallites in the tablet due to the mutual contact of the \*\*\*MePe\*\*\* -particles.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:311964 CAPLUS

DN 134:318532

TI The role of traps in the interpretation of Photo-E.M.F. parameters of organic dye pigments

AU Muller, F. W.; Damm, C.; Israel, G.

CS Martin-Luther-Universitat Halle-Wittenberg, Institut fur Organische Chemie, Merseburg, 06217, Germany SO Journal of Information Recording (2000), 25(5-6), 533-552

CODEN: JIREFL: ISSN: 1025-6008 PB Gordon & Breach Science Publishers

DT Journal

LA English

AB The decay of the transient Photo-ElectroMotive-Force U (Photo-E.M.F.) of org. dye pigments can be described as a biexponential process, even if the signals change the sign of U(t) within the decay. The dependencies of the four kinetic parameters U10; U20; k1 and k2 on wavelength and intensity of the exciting laser flash or addnl. continuous illumination were investigated using N,N'-Dimethylperylene-tetracarboxylic-bisimide ( \*\*\*MePe\*\*\* ) and Copper(II)-phthalocyanine (CuPc) as pigments dispersed in poly(vinyl butyral) (PVB) layers. In agreement with the trap concept of MOTT the type of cond. (nor p-type photoconduction) of \*\*\*MePe\*\*\* depends on the energy of the exciting light. CuPc does not show such a change of the photoconduction. More detailed information about the role of traps available for photogenerated charge carriers can be derived from time resolved Photo-E.M.F. expts. under addnl. continuous illumination of the sample by poly- and monochromatic light. The results show, that charge carriers involved in Photo-E.M.F. measurements will be influenced mainly by shallow traps (.DELTA.E in the meV-range). Occupation of traps by charge carriers generated under continuous illumination results in an increase of the decay rate for the faster process. This points out, that its parameters U10 and k1 may be attributed to a partial Photo-E.M.F. generated near the surface of the pigment particles.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:256780 CAPLUS

DN 135:47151

TI Layer-by-Layer self-assembly of a metallo-supramolecular coordination polyelectrolyte studied by infrared spectroscopy, microgravimetry, and X-ray reflectance

AU Kurth, Dirk G.; Schutte, Markus

CS Max-Planck-Institute of Colloids and Interfaces, Potsdam, D-14424, Germany

SO Macromolecular Symposia (2001), 164(Reactive Polymers), 167-179 CODEN: MSYMEC; ISSN: 1022-1360

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

AB Layer-by-Layer self-assembly on planar substrates of a Fe(II) metallo-supramol. coordination polyelectrolyte ( \*\*\*MEPE\*\*\* ) and poly(styrene sulfonate) (PSS) is investigated with a variety of surface sensitive techniques. Results from reflection-absorption IR (RAIR) spectroscopy and microgravimetry are in agreement with linear multilayer build-up. Furthermore, RAIR spectroscopy indicates close to complete counter ion exchange during polyion deposition. The multilayers contain approx. 20 mass-percent water under ambient conditions. Water uptake and loss is completely reversible. Annealing to 250.degree, in air does not affect the structural integrity of the film as demonstrated by x-ray reflectance (XRR) measurements.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2001:203836 CAPLUS

TI Metallo-supramolecular polyelectrolyte multilayers: Preparation, characterization, and properties AU Kurth, Dirk G.

CS Department of Interfaces, Max-Planck Institute of Colloids and Interfaces, Potsdam, 14476, Germany

SO Abstracts of Papers - American Chemical Society (2001), 221st, PMSE-138 CODEN: ACSRAL; ISSN: 0065-7727

PB American Chemical Society DT Journal; Meeting Abstract

LA English

AB A versatile approach is presented that allows incorporation of metallo-supramol. devices into layered architectures. Metal ion coordination of ditopic back-to-back bis-terpyridine ligands results in pos. charged metallo-supramol. coordination-polyelectrolytes ( \*\*\*MEPE\*\*\* ). Layer-by-layer self-assembly is utilized to immobilize MEPEs and neg. charged polyelectrolytes on solid substrates. We present results from reflection-absorption IR spectroscopy, microgravimetry, X-ray reflectance measurements, UV/vis absorption spectroscopy, as well as electrochem. studies. Multilayer build-up is linear and IR spectroscopy indicates a close to complete counter ion exchange during polyion deposition. With Co(II) as central metal ion we show that metal ions can be removed from the multilayer and that they can be replaced by Fe(II) ions. A second approach relies on complexation of MEPEs with suitable amphiphiles as a general method to tailor the surface chem. properties of these functional devices. The resulting polyelectrolyte-amphiphile complex (PAC) forms stable monolayers at the air-water interface with a bilayer structure, which is revealed by X-ray reflectance and X-ray diffraction studies. Finally, we show that PAC can form ordered selfassembled monolayers on graphite surfaces.

L3 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2000:578625 CAPLUS DN 134:1213

TI \*\*\*MEPE\*\*\*, a new gene expressed in bone marrow and tumors causing osteomalacia

AU Rowe, Peter S. N.; De Zoysa, Priyal A.; Dong, Rong; Wang, Huei Rong; White, Kenneth E.; Econs, Michael J.; Oudet, Claudine L.

CS Centre for Molecular Osteo-Renal Research, Department of Biochemistry and Molecular Biology, Royal Free and University College Medical School, London, NW3 2PF, UK SO Genomics (2000), 67(1), 54-68 CODEN: GNMCEP; ISSN: 0888-7543

**PB Academic Press** 

DT Journal

LA English

AB Oncogenic hypophosphatemic osteomalacia (OHO) is characterized by a renal phosphate leak, hypophosphatemia, lowserum calcitriol (1,25-vitamin-D3), and abnormalities in skeletal mineralization. Resection of OHO tumors results in remission of the symptoms, and there is evidence that a circulating phosphaturic factor plays a role in the bone disease. This paper describes the characterization and cloning of a gene that is a candidate for the tumor-secreted phosphaturic factor. This new gene has been named \*\*\*MEPE\*\*\* (matrix extracellular phosphoglycoprotein) and has major similarities to a group of bone-tooth mineral matrix phosphoglycoproteins (osteopontin (OPN; HGMW-approved symbol SPP1), dentin sialo phosphoprotein (DSPP), dentin matrix protein 1 (DMP1), bone sialoprotein II (IBSP), and bone morphogenetic proteins (BMP)). All the proteins including \*\*\*MEPE\*\*\* contain RGD sequence motifs that are proposed to be essential for integrin-receptor interactions. Of further interest is the finding that \*\*\*MEPE\*\*\* OPN, DSPP, DMP1, IBSP, and BMP3 all map to a defined region in chromosome 4g. Refined mapping localizes \*\*\*MEPE\*\*\* to 4q21.1 between ESTs D4S2785 (WI-6336) and D4S2844 (WI-3770). \*\*\*MEPE\*\*\* is 525 residues in length with a short Nterminal signal peptide. High-level expression of \*\*\*MEPE\*\*\* mRNA occurred in all four OHO tumors screened. Three of 11 non-OHO tumors screened contained trace levels of \*\*\*MEPE\*\*\* expression (detected only after RT-PCR and Southern 32P anal.). Normal tissue expression was found in bone marrow and brain with very-low-level expression found in lung, kidney, and human placenta. Evidence is also presented for the tumor secretion of clusterin (HGMW-approved symbol CLU) and its possible role as a cytotoxic factor in one of the OHO patients described. (c) 2000 Academic Press.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 2000:329324 CAPLUS

TI Thin films of metallosupramolecular coordination polyelectrolytes.

AU Kurth, Dirk G.

CS Max-Planck-Institute of Colloids and Interfaces, Potsdam, 14424, Germany

SO Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), COLL-063 Publisher: American Chemical Society, Washington, D. C. CODEN: 69CLAC DT Conference; Meeting Abstract

LA English

AB We present the integration of metallosupramol. functional units in structurally coherent, ultra thin polyelectrolyte interfaces. Metal ion coordination with back-to-back terpyridine ligands results in pos. charged metallosupramol. coordination-polyelectrolytes ( \*\*\*MEPE\*\*\* ). Layer-by-layer adsorption of MEPEs and neg. charged polyelectrolytes generates mol. films. This approach is extended to fabricate very large, sol., self-contained metallosupramol. entities employing a template-directed strategy based on charged nanoparticles. Electrostatic interactions of MEPEs and lipids result in metallosupramol.

polyelectrolyte-amphiphile complexes (PAC). The PAC forms a stable monolayer at the air-water interface that is readily transferred and oriented on solid supports with the Langmuir-Blodgett technique. The resulting material has a structure at several length scales. The presented study shows a novel route to integrate functional supramol. devices in mol. layers. The combination of different recognition motives (mol. recognition by metal ion coordination, electrostatic and hydrophobic interactions) permits the assembly of multilayered structures with interesting properties.

L3 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:753255 CAPLUS

DN 132:722

 $\Pi$  Cloning of human polypeptide hormone phosphatonin involved in phosphate metabolism

IN Rowe, Peter

PA University College London, UK

SO PCT Int. Appl., 136 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----

PI WO 9960017 A2 19991125 WO 1999-EP3403 19990518 WO 9960017 A3 20000309 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI. FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2329054 AA 19991125 CA 1999-2329054 19990518 AU 9943624 A1 19991206 AU 1999-43624 19990518 AU 765349 B2 20030918 GB 2339572 A1 20000202 GB 1999-11577 19990518 EP 1086225 A2 20010328 EP 1999-926320 19990518 R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI JP 2002515232 T2 20020528 JP 2000-549635 19990518

PRAI GB 1998-10681 A 19980518 GB 1998-19387 A 19980904 WO 1999-EP3403 W 19990518

AB The present invention relates to a novel human protein called phosphatonin (also known as \*\*\*Metastatic\*\*\* - \*\*\*tumor\*\*\* \*\*\*Excreted\*\*\* \*\*\*Phosphaturic\*\*\* -Element or \*\*\*MEPE\*\*\* ), and isolated polynucleotides encoding this protein. Phosphatonin modulates Na+-dependent phosphate co-transport, vitamin D metab. via renal 25-hydroxyvitamin D3 24-hydroxylase or 25-hydroxyvitamin D3 1.alpha.-hydroxylase, and/or bone mineralization. Phosphatonin was isolated from a cDNA library constructed form mRNA extd. from a meningeal phosphaturicmesenchymal-tumor resected from a patient suffering from oncogenic hypophosphatemic osteomalacia. The cDNA codes for a protein 430 amino acids in length. Phosphatonin may be cleaved proteolytically in vivo, for example by the PHEX metalloendopeptidase. Also provided are vectors, host cells, antibodies, and recombinant methods for producing this human protein. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to this novel human protein.

L3 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:680597 CAPLUS

DN 132:23459

 $\Pi$  Core-shell particles and hollow shells containing metallosupramolecular components

AU Caruso, Frank; Schueler, Corinna; Kurth, Dirk G.

CS Max Planck Institute of Colloids and Interfaces, Potsdam, D-14424, Germany

SO Chemistry of Materials (1999), 11(11), 3394-3399 CODEN: CMATEX; ISSN: 0897-4756

**PB American Chemical Society** 

DT Journal

LA English

AB Core-shell particles consisting of a polystyrene (PS) latex colloidal core and Fe(II) metallo-supramol. polyelectrolyte (Fe(II)- \*\*\*MEPE\*\*\* )/poly(styrenesulfonate) (PSS) multilayer shells were fabricated by the consecutive assembly of Fe(II)-\*\*\*MEPE\*\*\* and PSS on PS particles. The layers were deposited under conditions where the Fe(II)- \*\*\*MEPE\*\*\* and PSS are oppositely charged, thereby utilizing electrostatic attractions for multilayer buildup. Formation of Fe(II)- \*\*\*MEPE\*\*\* /PSS multilayers on weakly cross-linked melamine-formaldehyde (MF) particles, followed by MF particle decompn. and removal, resulted in hollow Fe(II)- \*\*\*MEPE\*\*\* /PSS shells. The Fe(II)-\*\*\*MEPE\*\*\* /PSS multilayer shell on the colloidal particles and the Fe(II)- \*\*\*MEPE\*\*\* /PSS hollow shells were found to be stable, resisting decompn. upon exposure to acidic solns, or chelating agents. PS latexes as small as 70 nm in diam, were also employed as templates for the successful fabrication of Fe(II)-\*\*\*MEPE\*\*\* /PSS and poly(allylamine hydrochloride)/PSS multilayer shells. These results demonstrate that our approach can be extended to colloidal templates with diams. less than 100 nm. This work represents a first study of structurally well-defined metallo-supramol, polyelectrolyte-colloid assemblies combining the functional units from supramol, chem, with the restricted dimensionality of colloids.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:512349 CAPLUS

DN 131:270831

TI Coexpression of CCR5 and IL-2 in human genital but not blood T cells: implications for the ontogeny of the CCR5+ Th1 phenotype

AU Hladik, Florian; Lentz, Gretchen; Delpit, Elizabeth; McElroy, Ami; McElrath, M. Juliana

CS Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109, USA

SO Journal of Immunology (1999), 163(4), 2306-2313 CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Memory T cells that home to inflamed tissues typically express the .beta.-chemokine receptor CCR5 and exhibit a Th1 cytokine profile. The migration of these cells into the genital tract following antigenic exposure has particular relevance to acquisition of HIV-1 infection, because CCR5 functions as the coreceptor for most sexually transmitted HIV-1 strains. We recently established methodol. to purify and culture mononuclear cells from the female reproductive tract, and here we analyzed the phenotype, CCR5 expression, and cytokine prodn. of cervicovaginal T cells in up to 16 donors. The proportion of mucosal T cells expressing CCR5 was markedly expanded as compared with peripheral blood (mean 88% vs 24% in 13 donors), but the receptor d. on individual CCR5+ T cells was only slightly increased (mean 5837 vs 4191 \*\*\*MEPE\*\*\* (mols. of equiv. PE) units in 6 of 7 donors). Intracellular costaining for IL-2, IFN-.gamma., IL-4, and IL-5 revealed a Th1-type pattern in cervical T cells, with significantly higher percentages of IL-2- and IFN-.gamma.-producing T cells in the mucosa than in blood (mean 67% vs 29%). Coexpression of surface CCR5 with

intracellular IL-2 and IFN-.gamma. was obsd. only among T cells in the mucosa, but not among those in circulation. Thus, we postulate that T cell homing to the genital mucosa leads to differentiation into the combined CCR5+ Th1 phenotype. Moreover, the predominance of CCR5+ Th1-type T cells in normal cervical mucosa provides targets accessible for the efficient transmission of macrophage-tropic HIV-1 variants in women following sexual exposure.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:479969 CAPLUS

DN 131:248728

TI Giant self-contained metallosupramolecular entities AU Kurth, Dirk G.; Caruso, Frank; Schuler, Corinna CS Max-Planck-Institute of Colloids and Interfaces, Potsdam, D-14424, Germany

SO Chemical Communications (Cambridge) (1999), (16), 1579-1580 CODEN: CHCOFS; ISSN: 1359-7345

PB Royal Society of Chemistry

DT Journal

LA English

AB The authors present an approach to fabricate very large, soi., self-contained metallosupramol. entities employing a template-directed strategy based on charged nanoparticles: consecutive deposition of neg. charged macromols. and pos. charged metallosupramol. coordination polyelectrolytes is exploited to assemble the metallosupramol. components on the nanoparticles. RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:328123 CAPLUS

DN 131:112517

TI Inhibition of agonist-induced vasocontraction and impairment of endothelium-dependent vasorelaxation by extract of motorcycle exhaust particles in vitro

AU Cheng, Yu-Wen; Kang, Jaw-Jou

CS Institute of Toxicology, College of Medicine, National Taiwan University, Taipei, Taiwan

SO Journal of Toxicology and Environmental Health, Part A (1999), 57(2), 75-87 CODEN: JTEHF8

PB Taylor & Francis

DT Journal

LA English

AB The in vitro effects of motorcycle exhaust particulate ext. ( \*\*\*MEPE\*\*\* ) on blood vessels were studied in thoracic aorta isolated from Wistar rat. The \*\*\*MEPE\*\*\* relaxed the phenylephrine-precontracted aorta with an EC50 value of 0.05 .+-. 0.004 mg/mL. This relaxing effect of \*\*\*MEPE\*\*\* persisted in endothelium-denuded aorta, suggesting that the relaxation induced by \*\*\*MEPE\*\*\* is endothelium-independent. The phenylephrine-induced vasocontraction and inositol 1,4,5triphosphate formation were inhibited concn. dependently in aorta pretreated with \*\*\*MEPE\*\*\* . However, the high K+induced vasocontraction and the Ca2+ sensitivity of the contractile proteins were not significantly affected by \*\*\*MEPE\*\*\* . In addn. to the inhibitory effects on agonistinduced contraction, the vasorelaxing effects both of acetylcholine and of sodium nitroprusside were impaired by \*\*\*MEPE\*\*\* . The inhibitory effects of \*\*\*MEPE\*\*\* on acetylcholine and sodium nitroprusside, but not phenylephrine, were reversed by cotreatment with superoxide dismutase. These results showed that the \*\*\*MEPE\*\*\*, added in vitro, inhibited the phenylephrine-induced, but not depolarization-induced, vasocontraction of the aorta. The \*\*\*MEPE\*\*\* also impaired the vasorelaxation induced by acetylcholine in a superoxide anion-dependent manner.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1999:256401 CAPLUS

DN 131:38295

TI Activation parameters of the photo-E.M.F. decay from N,N'-dimethylperylene- tetracarboxylic-bismide pigment

AU Damm, C.; Muller, F. W.; Israel, G.

CS Martin-Luther-Universitat Halle-Wittenberg, Institut fur Organische Chemie, Merseburg, D-06217, Germany SO Journal of Information Recording (1998), 24(5-6), 415-425

CODEN: JIREFL; ISSN: 1025-6008 PB Gordon & Breach Science Publishers

DT Journal

LA English

AB Simple Photo-E.M.F. decay curves and Photo-E.M.F.-signals with a sign reversal may be described by the same parameter set U10; U20; k1; k2 of a biexponential rate law. The 1st order decay consts. of both partial Photo-E.M.F.s k1 and k2 reflect the rate of the charge carrier transport and recombination. The temp. may mainly influence the charge carrier transport. Temp. dependent measurements of k1 and k2 of a fine dispersed N,N'-Dimethylperylene-tetracarboxylic-bisimide ( \*\*\*MePe\*\*\* ) in polyvinyl butyral (PVB) layer lead to the corresponding Arrhenius activation energies EA1 and EA2 at -240-+250 meV. Pos. values for EA1 and EA2 were found for the \*\*\*MePe\*\*\* -PVB layer up to T = 20.degree.(.lambda.exc=625 nm) and T =35.degree.(.lambda.exc=580 nm). Above these temps. EA1 remains pos., but EA2 becomes neg. This behavior is only partly in agreement with the simple MOTT-theory: According to the trap theory of MOTT in org. dye pigments the charge carrier transport occurs by hopping processes from a trap to another one. The promotion of charge carriers from traps into the bands needs an activation energy. Therefore the activation energies of k1 and k2 should correspond to an averaged depth of traps. The activation energies of k1 and k2 measured from fine dispersed \*\*\*MePe\*\*\*

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

embedded in PVB are in the meV range. Therefore one can say.

that the charge carrier transport takes place by hopping

L3 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1997:758208 CAPLUS

DN 128:68362

processes from shallow traps.

 $\Pi$  Measurement problems and kinetic treatment of photo-E.M.F. curves

AU Israel, G.; Muller, F. W.; Damm, C.; Harenburg, J. CS Institut fur Organische Chemie, Martin-Luther-Universitat Halle-Wittenberg, Merseburg, 06217, Germany SO Journal of Information Recording (1997), 23(6), 559-584 CODEN: JIREFL; ISSN: 1025-6008 PB Gordon & Breach Science Publishers DT Journal

DT Journal LA English

AB Signal/noise ratio and reproducibility of laser flash generated photo-emf. (photo-EMF) curves were improved by acquisition of several signals. This gives the opportunity of an exact kinetic treatment of the time resolved photo-EMF. A biexponential rate law U(t)=U10exp(-k1t) + U20exp(-k2t) allows the description of all kinds of exptl. signals. U10 and U20 were suggested as two hypothetical partial photo-EMF in the beginning, which can have equal or opposite signs. First order rate consts. k1 and k2 correspond to the two partial decay processes. In this way a very

good fit will be reached between measured and calcd. curves even in these cases, where the sign of the signal changes within the decay process (crossing point). Fine dispersed copper phthalocyanine (CuPc) and N,N'-dimethylperylenetetracarboxylic diimide (\*\*\*MePe\*\*\*) pigments in polyvinylbutyral layers as well as photog. silver halide emulsions were used as examples for p- and n-type photoconductors in order to proof the capability of the kinetic model. The dependence of the photo-EMF parameters on exptl. conditions such as flash intensity, film thickness, size of grains, and optical absorbance of the samples were investigated. RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN AN 1979:13876 CAPLUS

DN 90:13876

TI The ISEE 1 and 2 medium energy particles experiments AU Williams, D. J.; Keppler, E.; Fritz, T. A.; Wilken, B.; Wibberenz, G.

CS Space Environ. Lab., NOAAC, Boulder, CO, USA SO Report (1978), NOAA-TM-ERL-SEL-51, NOAA-78061209; Order No. PB-283350, 42 pp. Avail.: NTIS From: Gov. Rep. Announce. Index (U. S.) 1978, 78(18), 16

DT Report

LA English

AB The medium energy particles expt. ( \*\*\*MEPE\*\*\* ) on board ISEE 1 and 2 are described. The \*\*\*MEPE\*\*\* consists of the WIM instrument on ISEE1 and the KED instrument on ISEE 2: both instruments employ solid state detectors and magnetic anal. to measure the angular, energy, and intensity distributions of p >27 keV and e >20 keV. The WIM instrument also includes a compn. measurement employing .DELTA.E- E and time-of-flight techniques. Three parameter anal. is performed >250 keV/N, and single parameter anal. is performed >125 keV/N for He through O. Three-dimensional angular distributions were obtained through the use of a scan platform in the WIM instrument and multiple detector heads in the KED instrument. A variety of operational modes were used to optimize data collection from both instruments. Resolns. up to 128 channels in energy, 192 samples over the unit sphere in angle, and 0.095 s in time are available.

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